REMARKS

Claim 1, 5, 7 and 9 are amended. Support for the amendment to Claims 1 and 7 can be found in the specification, for example, at page 40, lines 2-6. Support for the amendment to Claims 5 and 9 can be found in the specification, for example, at page 22, lines 19 to 22; page 23, lines 10 to 13; and page 38, lines 8 to 23. No new matter is added by the amendments. Claims 1-12 are presently under examination.

Rejection under 35 U.S.C. § 112, first paragraph – Enablement

Claims 1-12 are rejected under 35 U.S.C. § 112, first paragraph because the specification allegedly does not support the full scope of the claims. Specifically, the Office Action states as follows:

> [T]he specification, while being enabling for a non-human animal model exhibiting prostate tissue damage characteristic of chronic nonbacterial prostatitis and a lower urinary tract disorder characteristically observed in chronic nonbacterial prostatitis wherein in the animal model is prepared by injection of hydrochloric acid(HCl), wherein the HCl concentration ranges from 0.1 N to 0.4 N, a method of using said nonbacterial prostatitis non-human animal model comprising administering a test substance and determining if it alleviates prostate tissue damage or lower urinary tract disorder symptoms, and a method of making said non-human prostatitis animal model comprising injecting HCl beneath the prostatic capsule wherein the HCl is between 0.1N and 0.4N, does not reasonably provide enablement for a nonbacterial prostatitis animal model produced using any concentration of HCl. *Office Action* at pages 2-3.

Applicants maintain that for at least the reasons of record, the claims as originally filed are fully enabled and it would not require undue experimentation to practice their full scope. Nevertheless, in the interest of advancing prosecution of the subject application, Claims 1 and 7 are amended to indicate that concentration of the hydrochloric acid ranges from 0.1N to 0.4N. Claims 2-6 and 8-12 depend therefrom. Thus, in accord with the position of the PTO, all claims as presently pending are fully enabled by the specification. Accordingly, Applicants respectfully request removal of this ground for rejection of the claims.

Rejection under 35 U.S.C. § 112, first paragraph

Claim 5 is rejected under 35 U.S.C. § 112, first paragraph as containing new matter because the specification allegedly only supports "about 4 days to about 1week", but the claims recite "4 days to 1 week".

Applicants submit that the wording of Claim 5 is fully supported by the teachings in the specification and the claims as originally filed. Nevertheless, in the interest of advancing prosecution, Claim 5 is amended to recite "4 days to 8 days." Claim 9 is similarly amended.

An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. See, *e.g.*, *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000). There is no *in haec verba* requirement under 35 U.S.C. § 112, first paragraph, and newly added claim limitations can be supported by the specification through express, implicit, or inherent disclosure. See, *e.g.*, *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996). If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. See, *e.g.*, *Vas-Cath, Inc. v.Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991); *Martin v. Johnson*, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972) (stating "the description need not be in *ipsis verbis* [*i.e.*, 'in the same words'] to be sufficient").

The present specification describes that preferable nonbacterial prostatitis animal models are those that have undergone at least 4 days, and more preferably at least 8 days of rearing after hydrochloric acid injection, on page 23, lines 10-13 in the specification. The present specification also describes that a nonhuman animal, which has undergone 8 days of rearing after hydrochloric acid injection, is preferable on page 22, lines 19-22 in the specification. The teachings of the specification make clear to those skilled in the art that the inventors were in possession of the claims as presently amended. Accordingly, the specification fully supports the amendment reciting "4 days to 8 days."

Rejection under 35 U.S.C. § 103

Claims 1-12 are rejected under 35 U.S.C. § 103 Claims 1-12 as obvious over Lang, Keetch, Fulmer, Robinette, and Royston in view of Goto. Specifically, the Office Action states that it would have been obvious to combine the teachings of Lang of administering an irritant to prostate to develop a model of prostatitis with the teachings of Keetch, Fulmer and Robinette of administering other compositions to develop a model of prostatitis, with the teachings of Royston

which teaches that HCl acts as a non-specific irritant and the teachings of Goto which teaches administration of HCl in developing a model of prostatitis.

Applicants respectfully traverse this rejection.

Applicants submit that the claimed nonbacterial prostatitis animal model is not obvious over the claimed references because no combination of these teaching would lead one to the presently claimed nonbacterial prostatitis model.

Claims

The presently claimed invention as amended above provides:

a nonbacterial prostatitis animal model exhibiting a prostate tissue damage characteristically observed in human chronic nonbacterial prostatitis and a lower urinary tract disorder characteristically observed in human chronic nonbacterial prostatitis, the animal model being a nonhuman animal, and being prepared by injecting hydrochloric acid beneath the prostatic capsule, wherein concentration of the hydrochloric acid ranges from 0.1N to 0.4N;

a method for preparing said nonbacterial prostatitis animal model comprising the steps of: injecting hydrochloric acid beneath the prostatic capsule of a nonhuman animal, and rearing the nonhuman animal to develop prostatitis; as well as

a method for screening for a substance for treating human chronic nonbacterial prostatitis comprising the steps of:

administering a test substance to the said nonbacterial prostatitis animal model, and

examining the effect of the test substance for ameliorating at least one disorder selected from the group consisting of a prostate tissue damage and a lower urinary tract disorder of the nonbacterial prostatitis animal model.

The presently claimed invention provides a unique animal model which exhibits tissue damage in the prostate tissue or the prostate and the surrounding tissue that is characteristically observed in human chronic nonbacterial prostatitis, and also exhibits a lower urinary tract disorder that is characteristically observed in human chronic nonbacterial prostatitis.

In order to achieve the above remarkable result, it is important that the animal model is prepared by injecting 0.1N to 0.4N hydrochloric acid beneath the prostatic capsule.

The Claims are not Obvious over Lang et al, Keetch et al, Fulmer et al., Robinette, and Royston in view of Goto

Relying on Lang et al, Keetch et al, Fulmer et al., Robinette, and Royston in view of Goto, the Office Action states that the instant invention is obvious.

As stated in the Office Action, none of Lang et al, Keetch et al, Fulmer et al., or Robinette, contemplate the use of HCl to induce prostatitis. In order to fill this gap, the Office Action cites Royston and Goto and states that use of the HCl is taught by Royston and Goto et al.

The animal model of the presently claimed invention produced by injecting hydrochloric acid in ranges from 0.1 N to 0.4 N beneath the prostatic capsule exhibits tissue damage in the prostate tissue or the prostate and the surrounding tissue that is characteristically observed in human chronic nonbacterial prostatitis as well as a pathology, *i.e.* bladder dysfunction such as a lower urinary tract disorder (pollakiuria, reduced effective bladder capacity (reduced volume of urine per urination), residual urine, etc.) that is characteristically observed in human chronic nonbacterial prostatitis.

In contrast, Lang et al, Keetch et al, Fulmer et al., Robinette, Royston, and Goto, alone or combined, provide model animals only having tissue damage, but do not refer to model animals also having a pathology of lower urinary tract disorder, *i.e.* dysfunction, because injected substances or the injected body parts are different.

Applicants below address the cited references. As is seen from the below, Applicants submit that the art as a whole, as represented by the combination of the cited references, provides model animals only having tissue damage, but does not provide model animals also having a pathology of lower urinary tract disorder, *i.e.* dysfunction, because injected substances or the injected body parts are different. Accordingly, the art as a whole does not render the claims obvious. For clarity of discussion of the combination of references, each reference is discussed in turn. The Office Action has indicated a concern that Applicants discuss in turn the references, which according to the Office Action, suggests that Applicants are requiring each reference to teach each limitation of the claims. Applicants herein attempt to address the art as a whole, but such requires pointing to that which is and that which is not present in all cited references. For purposes of most clearly presenting their position, Applicants address the teachings of each reference in turn. In addition, Applicants discuss the teachings of the references when combined. As is seen from the below, the art as a whole does not render the claims obvious.

Specifically, Lang et al. only describes that animal models were produced by injecting ethanol into the ventral prostate of male rats to reduce mucosal integrity and adding dinitrobenzenesulfonic acid; and histological examinations and measurement of interleukin-1β levels thereof showed that the animal models developed inflammation, *i.e.* tissue damage in their prostates (Lang et al., page 202 "Animal Model"; page 203 "Histological Examination" and

"Cytokine Levels"). However, Lang et al. does not describe a nonbacterial animal model exhibiting both prostate tissue damage as well as dysfunctions such as lower urinary tract disorder.

Keetch et al. only describes that animal models were produced by injecting homogenates into the prostate tissues of syngeneic mice; and histological examinations thereof showed that the animal models developed inflammation, *i.e.*, tissue damage in their prostates (Keetch et al., page 247, "ABSTRACT"; right column, page 247, "Histopathology"; and page 249, lines 51-53). However, Keetch et al. does not describe a nonbacterial animal model exhibiting both prostate tissue damage as well as dysfunctions such as lower urinary tract disorder.

Combination of Lang et al. with Keetch et al. might lead to a combination of injected materials that cause prostate tissue damage, but there is no guidance provided in the combination of references that would lead one of ordinary skill to develop a nonbacterial animal model exhibiting both prostate tissue damage as well as dysfunctions such as lower urinary tract disorder.

Fulmer et al. only describes that animal models were produced by injecting lipopolysaccharide; and histological examinations thereof showed that the animal models developed inflammation, *i.e.*, tissue damage in their prostates (Fulmer et al., page 248, "ABSTRACT"; page 249, left column, lines 34-36 and 40-43; and page 249, right column, lines 15-20 from the bottom). However, Fulmer et al. does not describe a nonbacterial animal model exhibiting both prostate tissue damage as well as dysfunctions such as lower urinary tract disorder.

Combination of Lang et al. and/or Keetch et al. with Fulmer et al. might lead to a combination of injected materials that cause prostate tissue damage, but there is no guidance provided in any combination of these references that would lead one of ordinary skill to develop a nonbacterial animal model exhibiting both prostate tissue damage as well as dysfunctions such as lower urinary tract disorder.

Robinette only describes that animal models were produced by injecting estradiol into castrated rats; and histological examinations thereof showed that the animal models developed inflammation, *i.e.* tissue damage in their prostates (Robinette, page 271, "abstract"; page 273, lines 3 to page 274, lines 13; page 275, lines 3-5 and 16-19; and page 284, lines 18-21). However, Robinette does not describe a nonbacterial animal model exhibiting both prostate tissue damage as well as dysfunctions such as lower urinary tract disorder.

Combination of Lang et al. and/or Keetch et al. and/or Fulmer et al. with Robinette might lead to a combination of injected materials that cause prostate tissue damage, but there is no guidance provided in any combination of these references that would lead one of ordinary skill to

develop a nonbacterial animal model exhibiting both prostate tissue damage as well as dysfunctions such as lower urinary tract disorder.

Royston describes that in animal models produced by injecting hydrochloric acid of pH1 and pH2 into the lungs of rats, there was a increase in 99mTcDTPA clearance and also in lung wet:dry weight ratio; and oedema formation in the lung is just suggested thereby (Royston, abstract). However, Royston does not describe a nonbacterial animal model exhibiting both prostate tissue damage as well as dysfunctions such as lower urinary tract disorder, because the HCl-injected body part is totally different.

Clearly, Royston provides no guidance as to how or if HCl can be injected into prostate so as to lead to a nonbacterial animal model exhibiting both prostate tissue damage as well as dysfunctions such as lower urinary tract disorder. As discussed above, such guidance also is lacking in any combination of Lang et al. and/or Keetch et al. and/or Fulmer et al. and/or Robinette. Accordingly, combination of Lang et al. and/or Keetch et al. and/or Fulmer et al. and/or Robinette with Royston might lead to a combination of injected materials that might include HCl and that cause prostate tissue damage, but there is no guidance provided in any combination of these references that would lead one of ordinary skill to develop a nonbacterial animal model exhibiting both prostate tissue damage as well as dysfunctions such as lower urinary tract disorder.

Goto only describes that in animal models produced by inoculating bacteria such as *Escherichia coli* after pretreatment injection of hydrochloric acid into the vas deferens, prostatitis was induced bacteriologically and histopathologically. Further, as acknowledged by the Office Action, Goto's teaching of injection of HCl resulted in "only slight prostatitis." *Office Action* at page 11. Goto's "only slight prostatitis" is in contrast to Applicants' claimed nonbacterial prostatitis model which exhibits a prostate tissue damage characteristically observed in human chronic nonbacterial prostatitis and a lower urinary tract disorder characteristically observed in human chronic nonbacterial prostatitis, where the model is prepared by injecting hydrochloric acid beneath the prostatic capsule, wherein concentration of the hydrochloric acid ranges from 0.1N to 0.4N. Thus, consistent with the Office Action's position on Goto, at most Goto describes a bacterial prostatitis animal model and an "only slight prostatitis" animal model, but Goto does not describe any nonbacterial animal model exhibiting both prostate tissue damage as well as dysfunctions such as lower urinary tract disorder.

Goto's bacterial prostatitis animal model and "only slight prostatitis" animal model adds nothing to that which is lacking in any combination of Lang et al. and/or Keetch et al. and/or Fulmer

et al. and/or Robinette and/or Royston. Combination of Lang et al. and/or Keetch et al. and/or Fulmer et al. and/or Robinette and/or Royston with Goto might lead to a combination of injected materials that might include *E. coli* and optionally also HCl and that cause prostate tissue damage, but there is no guidance provided in any combination of these references that would lead one of ordinary skill to develop a nonbacterial animal model exhibiting both prostate tissue damage as well as dysfunctions such as lower urinary tract disorder.

In view of the above, none of the references, alone or combined, provide sufficient guidance to direct one of ordinary skill to develop a nonbacterial animal model exhibiting both prostate tissue damage as well as dysfunctions such as lower urinary tract disorder. Furthermore, it is generally known that animal models that have tissue damage do not necessarily reproduce human pathology. Therefore, a person skilled in the art when considering the whole of the descriptions of the all cited references would not have known how to develop an animal model exhibiting a pathology of lower urinary tract disorder, etc. (pollakiuria, reduced effective bladder capacity (reduced volume of urine per urination), residual urine, etc.), *i.e.* bladder dysfunction that is characteristically observed in human chronic nonbacterial prostatitis. In view of the foregoing, the instant invention as defined in amended Claim 1 is unobvious over any combination the cited references by Lang et al, Keetch et al, Fulmer et al., Robinette, and Royston in view of Goto.

Claims 2 to 12 also are Non-Obivous

Claims 2 to 6 are dependent on Claim 1. Further, the inventions recited in Claims 7 to 10 relate to a method for producing the animal model recited in Claim 1. Moreover, the invention recited in Claim 12 is a method of screening for a substance so as to treat human chronic nonbacterial prostatitis, which essentially requires using the animal model of Claim 1.

Therefore, Claims 2 to 12 are non-obvious over the references for the same reason as described above.

CONCLUSION

In view of the above, Applicants respectfully maintain that claims are patentable and request that they be passed to issue. Applicants invite the Examiner to call the undersigned if any remaining issues might be resolved by telephone.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: May 18, 2007 By: _____

Kerry Taylor
Registration No. 43,947
Attorney of Record
Customer No. 20,995
(619) 235-8550

3776802
051607